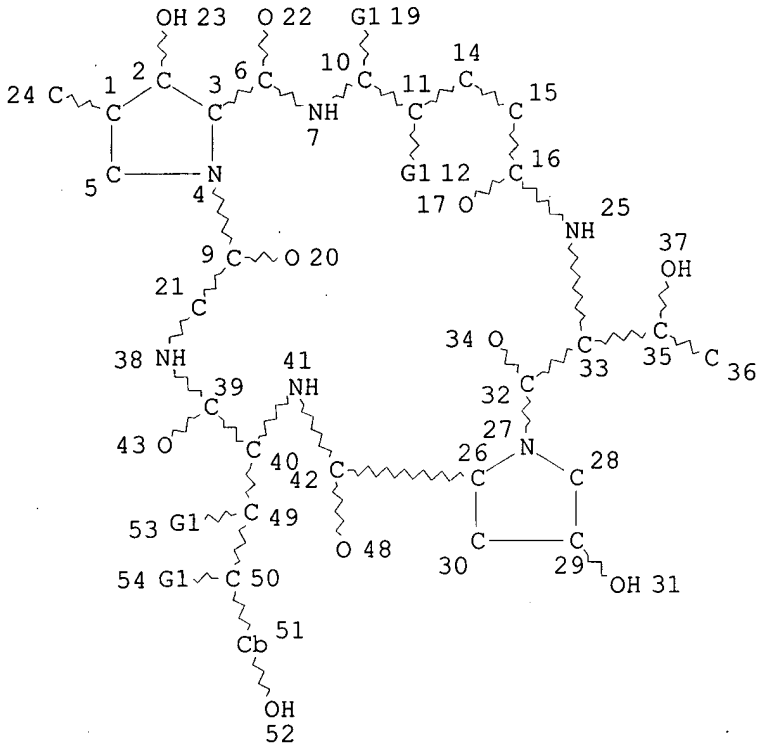
Mohamed, A.
09/673836

(FILE 'REGISTRY' ENTERED AT 12:14:05 ON 17 OCT 2002)

L5 STR

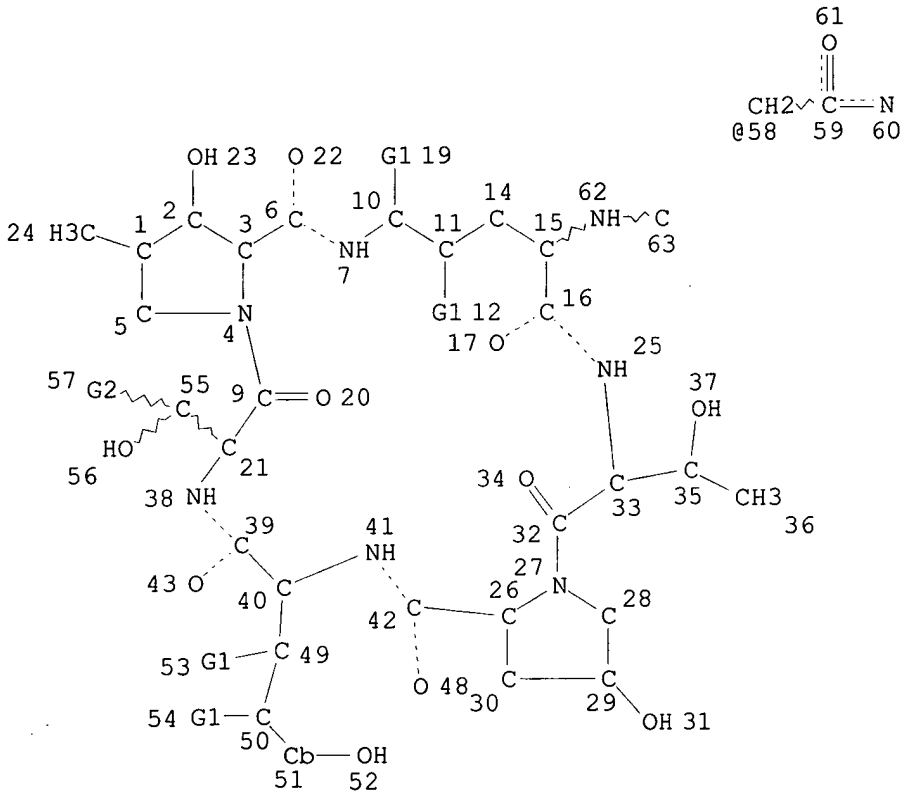


Str. Claim 1

VAR G1=H/OH
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 51
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
L7 1919 SEA FILE=REGISTRY SSS FUL L5
L22 STR



VAR G1=H/OH
VAR G2=H/CH3/58
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 51
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
L23 1861 SEA FILE=REGISTRY SUB=L7 SSS FUL L22
L24 314 SEA FILE=REGISTRY ABB=ON PLU=ON L23 AND NR=4

(FILE 'HCAPLUS' ENTERED AT 12:23:39 ON 17 OCT 2002)
L25 99 S L24/P

FILE 'REGISTRY' ENTERED AT 12:29:56 ON 17 OCT 2002
E "C4-HOMOTYROSINE"/CN 5
E "C4-HTYR"/CN 5

FILE 'HCAPLUS' ENTERED AT 12:30:23 ON 17 OCT 2002
L26 1 S L25 AND (C4(W)(HTYR OR (H OR HOMO)(W)(TYR OR TYROSINE))

(FILE 'REGISTRY' ENTERED AT 12:37:53 ON 17 OCT 2002)
E RANEY NICKEL/CN 5

* See last pgs. for term C4-homotyrosine

L39 1 S E3

FILE 'HCAPLUS' ENTERED AT 12:37:58 ON 17 OCT 2002
L40 2 S L25 AND (L39 OR RANEY(W)(NICKEL OR NI))

=> s l26 or l40
L41 2 L26 OR L40

=> sel hit l41 1-2 rn
E1 THROUGH E7 ASSIGNED

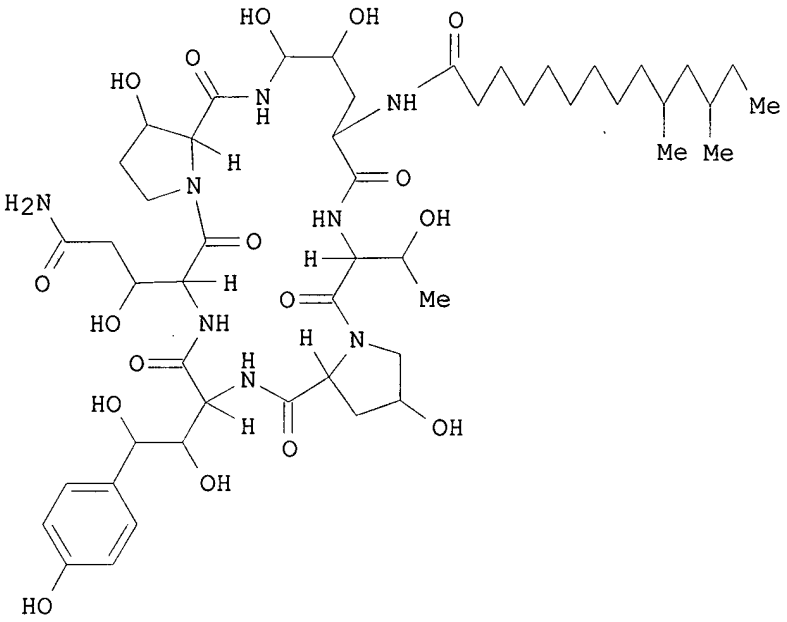
=> d 1-2 ibib abs hitstr

L41 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:117192 HCAPLUS
DOCUMENT NUMBER: 132:165211
TITLE: Method for the production of an antibiotic agent
INVENTOR(S): Connors, Neal C.; Petersen, Leslie A.; Hughes, David L.; Dimichele, Lisa M.; Novak, Thomas J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000008197	A1	20000217	WO 1999-US17444	19990804
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953311	A1	20000228	AU 1999-53311	19990804
EP 1100947	A1	20010523	EP 1999-938933	19990804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-95691P P 19980807
WO 1999-US17444 W 19990804

GI



I

AB An improved process for prepg. the compd. of formula (I) is disclosed which utilizes certain amino acids and divalent cations such as Ni, Co, and Zn to increase titer and decrease the amt. of structural analogs.

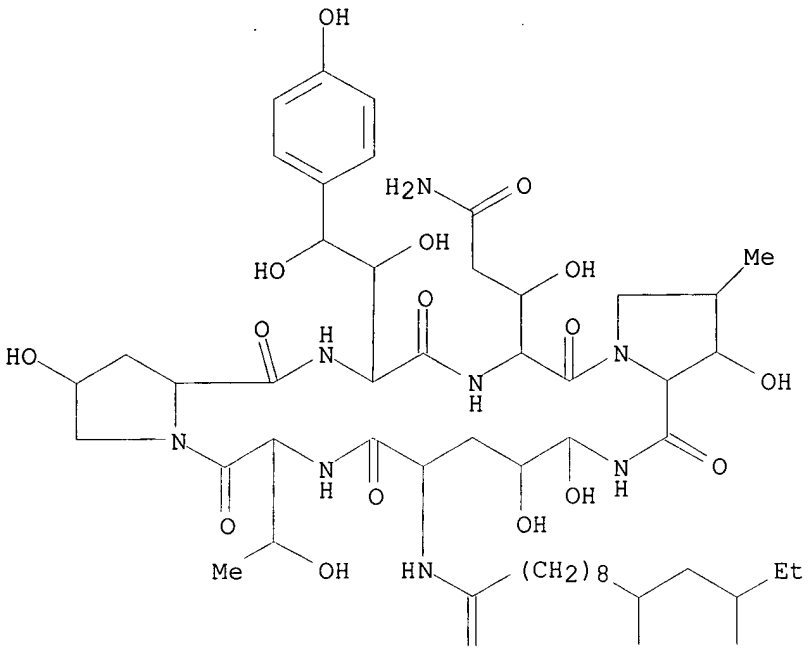
IT **120692-19-5P**, Pneumocandin A0
RL: BAC (Biological activity or effector, except adverse); BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(prodn. of antibiotic agents by Glarea)

RN 120692-19-5 HCAPLUS

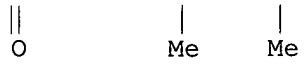
CN Pneumocandin A0 (9CI) (CA INDEX NAME)

Currently available stereo shown.

PAGE 1-A



PAGE 2-A



IT **7440-02-0**, Nickel, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(prodn. of antibiotic pneumocandin derivs. with Glarea lozoyensis)
RN 7440-02-0 HCAPLUS
CN Nickel (8CI, 9CI) (CA INDEX NAME)

Ni

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:708788 HCAPLUS
DOCUMENT NUMBER: 131:322923
TITLE: A process for the conversion of echinocandin class of peptides to their C4-homotyrosine monodeoxy analogs

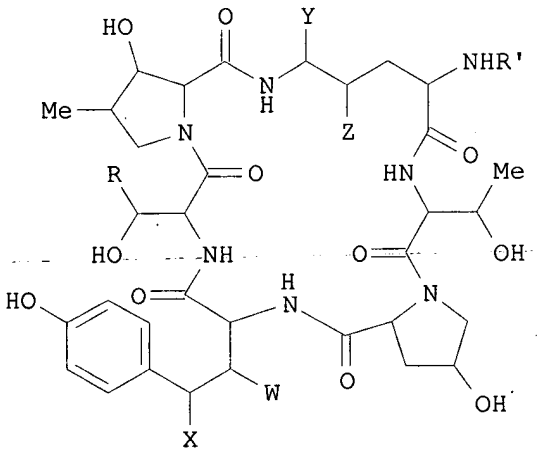
Searcher : Shears 308-4994

INVENTOR(S): Mukhopadhyay, Triptikumar; Jayvanti, Kenia; Kumar, Erra Koteswara Satya Vijaya
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955727	A1	19991104	WO 1999-EP2715	19990422
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2327474	AA	19991104	CA 1999-2327474	19990422
AU 9937096	A1	19991116	AU 1999-37096	19990422
BR 9909853	A	20001219	BR 1999-9853	19990422
EP 1073675	A1	20010207	EP 1999-919261	19990422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002513033	T2	20020508	JP 2000-545885	19990422
NO 2000005258	A	20001019	NO 2000-5258	20001019

PRIORITY APPLN. INFO.: EP 1998-107397 A 19980423
WO 1999-EP2715 W 19990422

OTHER SOURCE(S): CASREACT 131:322923; MARPAT 131:322923
GI



I

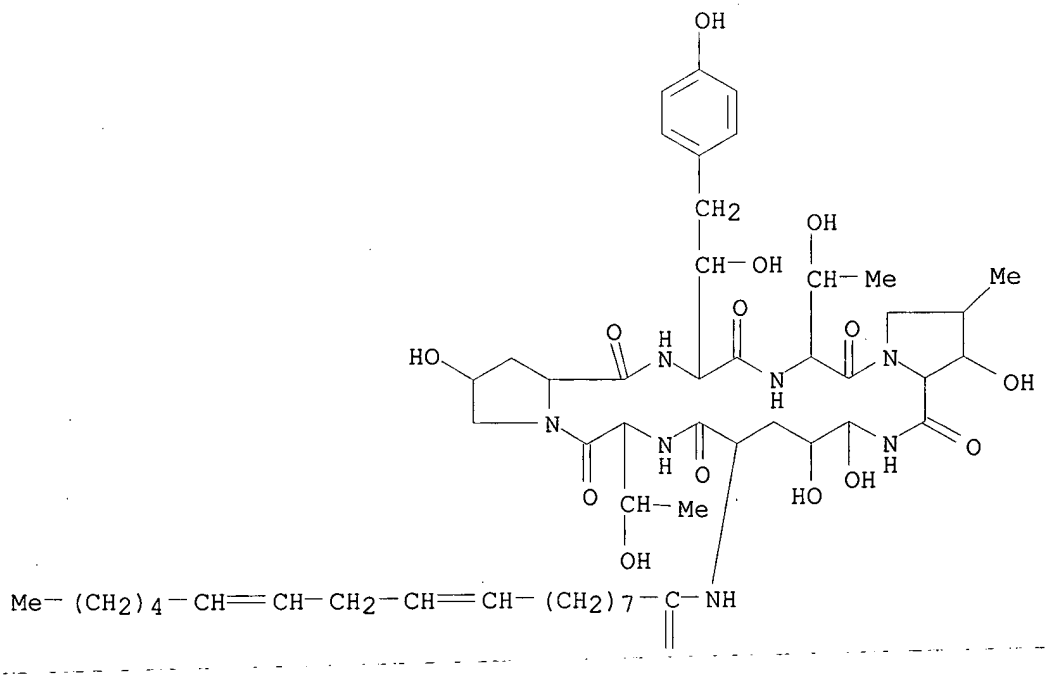
AB Echinocandin type peptides I (X = OH; W, Y, Z = OH, H; R = Me,

CH2CONH2, H; R' = linoleoyl, 10,12-dimethylmyristoyl, 12-methyltetradecanoyl) were converted to their C4-homotyrosine (**C4-htyr**) monodeoxy analogs I (X = H) via a single step selective redn. of the **C4-htyr** hydroxyl group of echinocandins to their monodeoxy analogs under neutral conditions without prior protection/deprotection of the equally facile C5-Orn (ornithine) hydroxyl group and purifn. of the monodeoxy compd. from the crude reaction mixt. Thus, a mixt. of mulundocandin and **Raney nickel** in a pH 7 ethanol soln. was stirred for 3 h at room temp. to afford 30% deoxymulundocandin, following purifn. by liq.-liq. chromatog.

IT **71018-12-7P**, Echinocandin c **138626-63-8P**, Deoxymulundocandin **144476-69-7P**, Deoxypneumocandin A2 **248281-21-2P**, Deoxypneumocandin A0 **248281-23-4P**, Deoxypneumocandin A1
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for conversion of echinocandin class of peptides to their C4-homotyrosine monodeoxy analogs)

RN 71018-12-7 HCAPLUS
CN Echinocandin C (9CI) (CA INDEX NAME)

PAGE 1-A

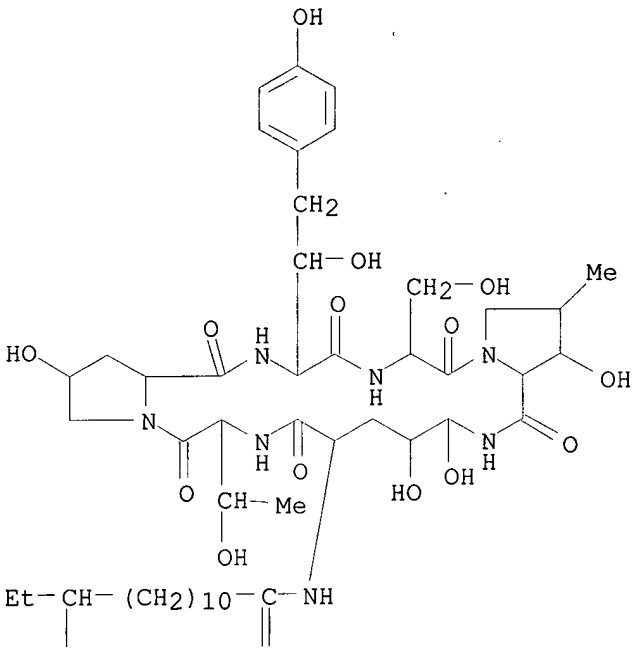


PAGE 2-A

RN 138626-63-8 HCAPLUS

CN Deoxymulundocandin (9CI) (CA INDEX NAME)

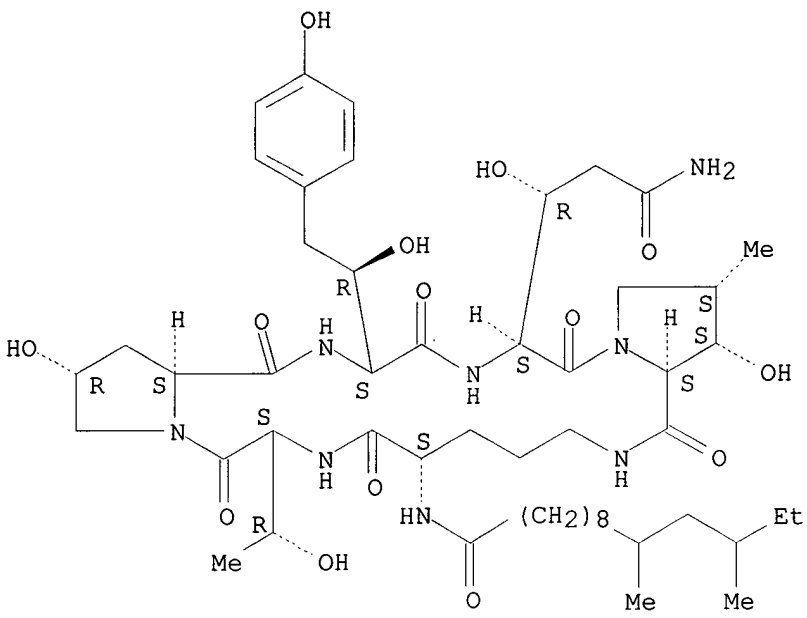
PAGE 1-A



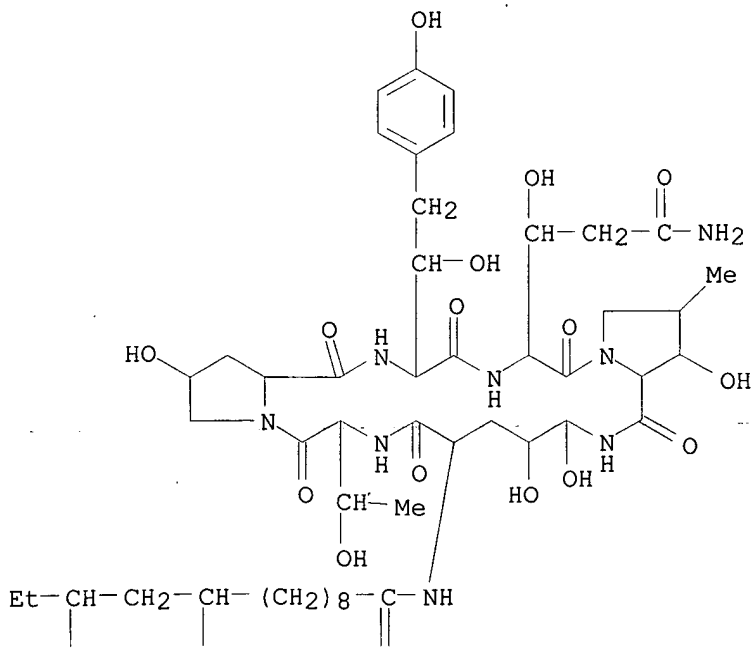
PAGE 2-A

RN 144476-69-7 HCAPLUS
CN Pneumocandin A2, 4-[4-(4-hydroxyphenyl)-L-threonine]- (9CI) (CA INDEX NAME)

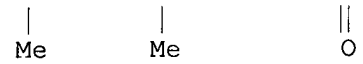
Absolute stereochemistry.



RN 248281-21-2 HCAPLUS
CN Pneumocandin A0, 4-[4-(4-hydroxyphenyl)-L-threonine]- (9CI) (CA INDEX NAME)

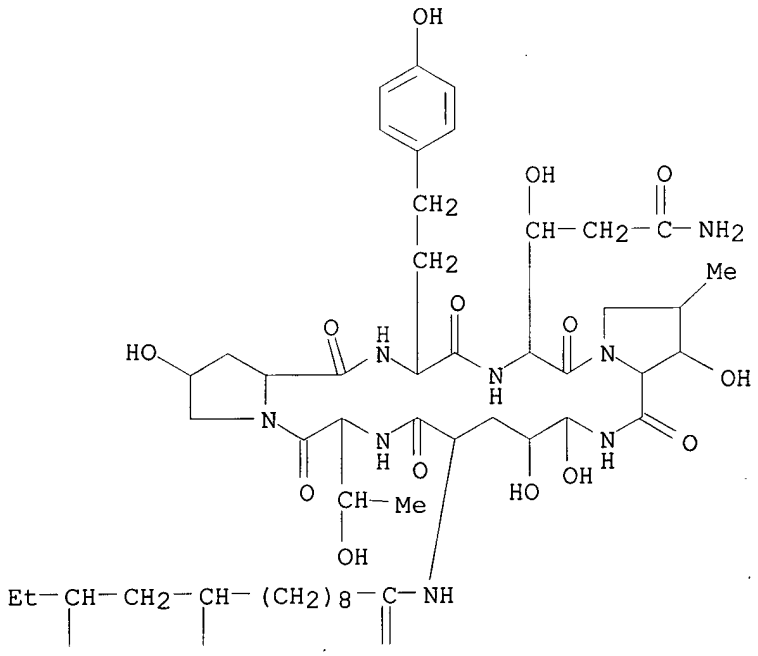


PAGE 2-A



RN 248281-23-4 HCAPLUS
CN Pneumocandin A0, 4-[(.alpha.S)-.alpha.-amino-4-hydroxybenzenebutanoic acid]- (9CI) (CA INDEX NAME)

PAGE 1-A



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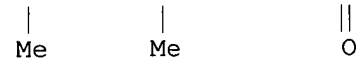


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'REGISTRY' ENTERED AT 12:41:37 ON 17 OCT 2002
L42 7 SEA FILE=REGISTRY ABB=ON PLU=ON (120692-19-5/BI OR 138626-63-8/BI OR 144476-69-7/BI OR 248281-21-2/BI OR 248281-23-4/BI OR 71018-12-7/BI OR 7440-02-0/BI)

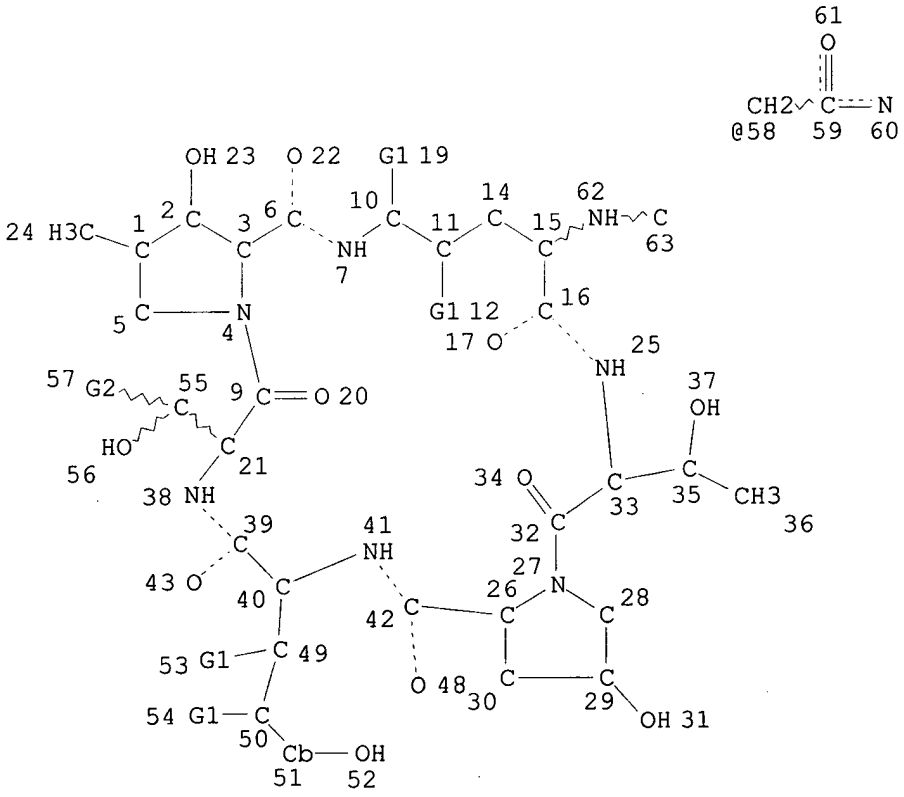
FILE 'CAOLD' ENTERED AT 12:41:53 ON 17 OCT 2002
L43 0 S L42

Searcher : Shears 308-4994

(FILE 'USPATFULL' ENTERED AT 12:42:01 ON 17 OCT 2002)
L44 1300 SEA ABB=ON PLU=ON L42/P
L45 0 SEA ABB=ON PLU=ON L44 AND (C4(W)(HTYR OR (H OR HOMO)(W)(TYR OR TYROSINE)))

L50 1288 S L44(S)(L39 OR RANEY(W)(NICKEL OR NI))
L51 0 S L50(S)(REDUC? OR RED#)

(FILE 'CASREACT' ENTERED AT 12:47:10 ON 17 OCT 2002)
L22 STR



VAR G1=H/OH
VAR G2=H/CH3/58
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 51
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
L53 14 SEA FILE=CASREACT SSS FUL L22 (217 REACTIONS)

100.0% DONE 391 VERIFIED 217 HIT RXNS 14 DOCS
SEARCH TIME: 00.00.01

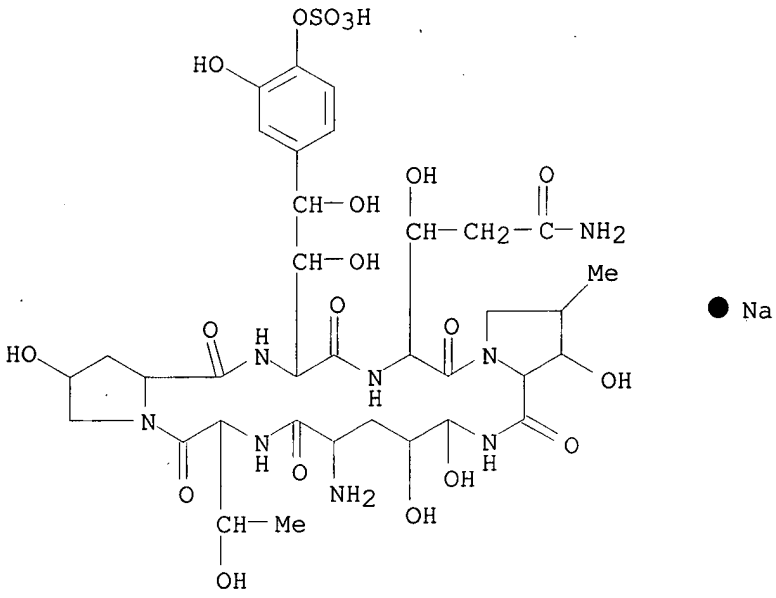
L53 ANSWER 1 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:296085 CASREACT
TITLE: FR131535, a novel water-soluble echinocandin-like lipopeptide: synthesis and biological properties
AUTHOR(S): Fujie, A.; Iwamoto, T.; Sato, B.; Muramatsu, H.; Kasahara, C.; Furuta, T.; Hori, Y.; Hino, M.; Hashimoto, S.
CORPORATE SOURCE: Exploratory Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Ibaraki, Tsukuba-shi, 300-2698, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 399-402
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and biol. properties of a novel water-sol. echinocandin-like lipopeptide, FR131535, are described. This compd. displayed potent in vitro and in vivo antifungal activities. The hemolytic activity of FR901379 was reduced by replacing the acyl side chain. This compd. showed good water-soly., comparable to the natural product FR901379. The synthesis and biol. properties of a novel water-sol. echinocandin-like lipopeptide FR131535 are described.

RX(1) OF 10 **A** ===> B...

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



B

RX(1) RCT A **138328-74-2**
PRO B 334541-91-2
NTE literature prepn.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 2 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:131818 CASREACT
TITLE: Preparation of novel cyclohexapeptides based on mulundocandin for use as antifungal agents
INVENTOR(S): Bansi, Lal; Vitthal, Genbhau Gund; Ashok, Kumar Gangopadhyay
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007468	A2	20010201	WO 2000-EP6769	20000715
WO 2001007468	A3	20011108		

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1204677 A2 20020515 EP 2000-953050 20000715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: EP 1999-114649 19990727
WO 2000-EP6769 20000715
OTHER SOURCE(S): MARPAT 134:131818

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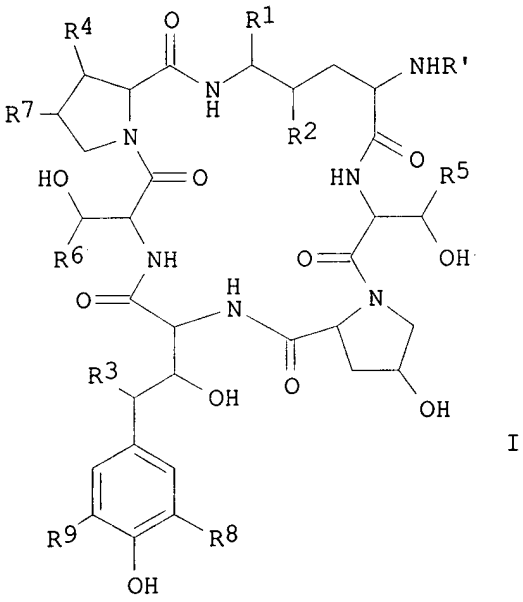


I

AB Cyclohexapeptides I [R' = alkyl, alkenyl, Ph, biphenyl, terphenyl, naphthyl, alkyl-, alkenyl-, or alkoxyphenyl, linoleoyl, palmitoyl, 12-methylmyristoyl, 10,12-dimethylmyristoyl, or COC6H4OC8H17-p; R1, R3 = OH, CN, CH2NH2, N3, (un)substituted aryl or heterocyclyl with 1-3 of the same or different heteroatoms, aminoalkylamino, (un)substituted alkoxy, etc.; R2, R4 = H, OH; R5 = H, Me; R6 = H, Me, CH2CONH2; R7 = H, Me, OH; R8, R9 = H or secondary aminomethyl] or their pharmaceutically acceptable salts were prepd. for use as antifungal agents. Thus, mulundocandin underwent mono- and dibenzylation on treatment with benzyl alc. and a catalytic amt. of p-toluenesulfonic acid in 1,4-dioxane. Ornithine-5-benzylmulundocandin underwent Mannich reaction with a various secondary amines.

RX(1) OF 69 2 **A** + 3 B ===> C + D...

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

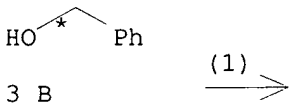
PAGE 2-A

A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

A



3 B

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

C
YIELD 67%

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

D
YIELD 13%

RX(1) RCT A **108351-20-8**, B 100-51-6

STAGE(1)
CAT 104-15-4 TsOH
SOL 123-91-1 Dioxane

STAGE(2)
RGT E 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO C 321660-96-2, D 321745-36-2

L53 ANSWER 3 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:17732 CASREACT
TITLE: Novel echinocandin derivatives, method for preparing same and use as antifungal agents
INVENTOR(S): Corbier, Alain; Fauveau, Patrick; Pietre-Dischamp, Nathalie; Schio, Laurent; Vicat, Pascale
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Fr.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075178	A1	20001214	WO 2000-FR1569	20000608
W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2794747	A1	20001215	FR 1999-7252	19990609
EP 1189932	A1	20020327	EP 2000-940456	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			FR 1999-7252	19990609
			WO 2000-FR1569	20000608

OTHER SOURCE(S): MARPAT 134:17732
GI

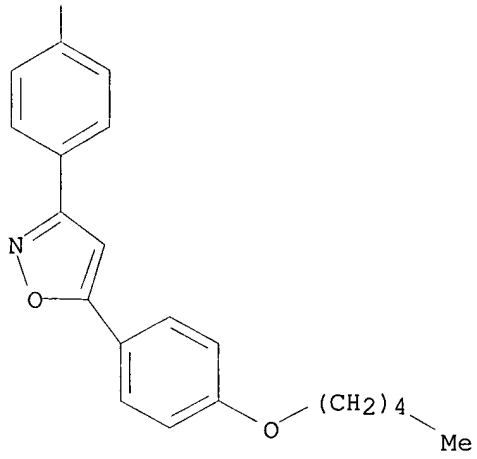
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention concerns cyclic peptides I wherein: R = chain contg. up to 30 carbon atoms, optionally contg. one or several heteroatoms, one or several heterocycles; either R1 and R2 = H, OH, alkyl optionally substituted, or NR1 forms with the carbon bearing NR1R2 a double bond and R2 is XRa, X being O, NH or N-alkyl and Ra being H, alkyl optionally substituted; R3 = H, OH, CH3; R4 = H, OH; T = H, CH3, CH2CONH2, CH2CN, (CH2)2NH2; Y = H, OH, halogen, OSO3H; W = H, OH; Z = H or CH3. The products of formula I have antifungal properties. Thus, trans-1-[4-[(2-aminocyclo-hexyl)amino]-N2-[[4-[5-[4-(pentyloxy)phenyl]-3-isoxazolyl]phenyl]carbonyl]-L-ornithine]-4-[4-(4-hydroxyphenyl)-L-threonine]-5-L-serine-echinocandin B trifluoroacetate was prepd. and tested for its inhibition of glucan synthase of Candida albicans.

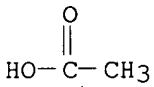
RX(1) OF 28 ...2 A + 2 B + 2 C ===> **D** + E

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



2 A



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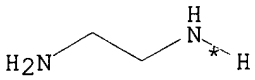
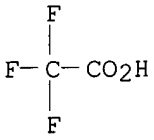
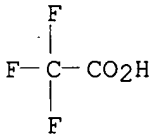


2 B: CM 2



2 C

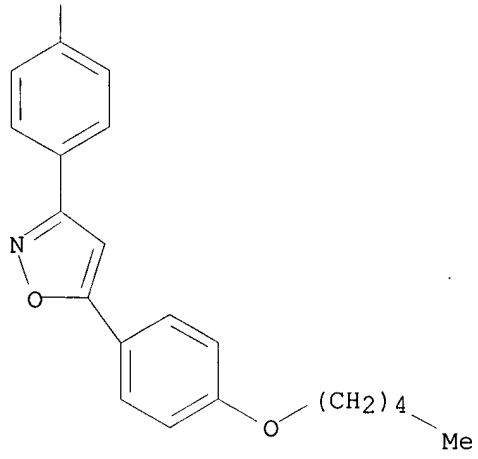
(1) →



D: CM 1

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



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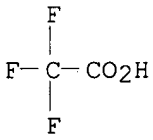
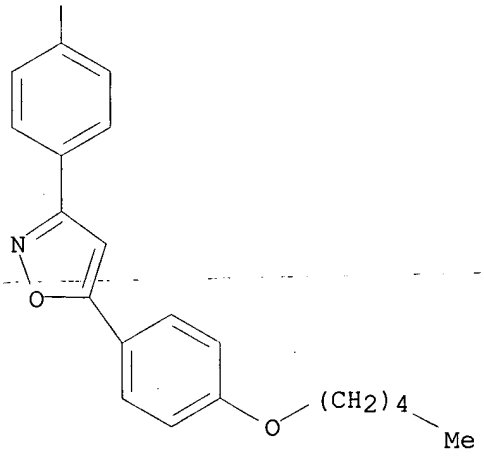


E: CM 1

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



E: CM 2

RX(1) RCT A 310459-17-7, B 38734-69-9

STAGE(1)
RGT F 25895-60-7 NaBH3CN
SOL 67-56-1 MeOH

STAGE(2)
RCT C 76-05-1
SOL 7732-18-5 Water, 75-05-8 MeCN
PRO D **310459-08-6**, E 310459-11-1
NTE 4A mol. sieves; last step semi-preparative HPLC
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 4 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:17731 CASREACT
TITLE: Echinocandin derivatives, method for preparing same and application as glucan synthase inhibitors and antifungal agents
INVENTOR(S): Fauveau, Patrick; Hawser, Stephen; Lebourg, Gilles; Schio, Laurent
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Fr.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075177	A1	20001214	WO 2000-FR1568	20000608
W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2794746	A1	20001215	FR 1999-7251	19990609
EP 1189933	A1	20020327	EP 2000-942169	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			FR 1999-7251	19990609
			WO 2000-FR1568	20000608

OTHER SOURCE(S): MARPAT 134:17731
GI

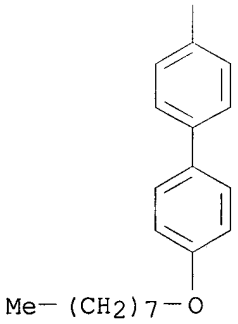
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention concerns in all possible isomeric forms as well as their mixts., cyclic peptides I wherein: R represents a linear,

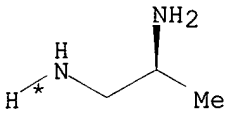
branched or cyclic chain; either R1 represents H or CH3 and R2 represents cyclohexyl substituted by an amine, cyanoalkyl ; or R1 and R2 form with the nitrogen which bears them a cycle with 3, 4 or 5 carbons optionally substituted by an amine; R3 represents hydrogen, Me or hydroxyl; R4 represents hydrogen or hydroxyl; T represents hydrogen, Me, CH2CONH2, CH2CN, a (CH2)2NH2 or (CH2)2Nalk+X- radical, X being halogen and alk an alkyl radical; Y represents hydrogen, hydroxyl, halogen or OSO3H; W represents H or OH; Z represents H, CH3. The compds. of formula I have antifungal properties. Thus,. Trans 1-[4-[(2-aminocyclohexyl)amino]-N2-[[4''-(pentyloxy)[1,1':4',1''terphenyl]-4-yl]carbonyl]-L-ornithine]-4-[4-(4-hydroxyphenyl)-L-threonine]-5-L-serine-echinocandine B trifluoroacetate was prepd. and tested for its inhibition of glucan synthase of Candida albicans and of the enzyme prepd. from Aspergillus fumigatus.

RX(1) OF 12 ...2 A + 2 B + 2 C ===> **D** + E

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

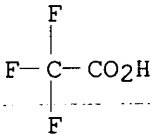


2 A



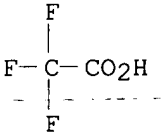
●2 HCl

2 B



2 C

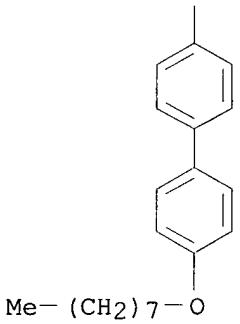
(1)



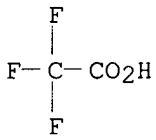
D: CM 1

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



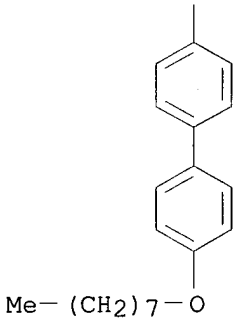
D: CM 2



E: CM 1

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



E: CM 2

RX(1) RCT A 227472-55-1, B 19777-66-3

STAGE(1)
RGT F 121-44-8 Et3N
SOL 67-56-1 MeOH

STAGE(2)
RGT G 25895-60-7 NaBH3CN

Searcher : Shears 308-4994

STAGE(3)
RCT C 76-05-1
SOL 7732-18-5 Water, 75-05-8 MeCN
PRO D **310461-86-0**, E 310461-89-3
NTE 1st stage siliporite grains; last stage semi-preparative HPLC

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 5 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 132:308664 CASREACT
TITLE: Photochemical process for conversion of the 1,2-diol moiety of an echinocandin compound to the 1-deoxy-2-keto analog
INVENTOR(S): Hitchcock, Stephen Andrew; Gregory, George Stuart
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024694	A1	20000504	WO 1999-US25301	19991027

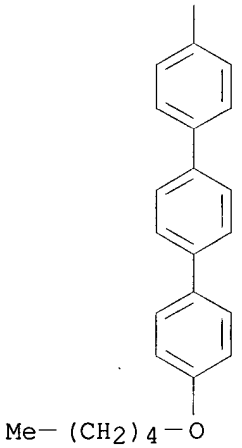
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-105936P 19981028
OTHER SOURCE(S): MARPAT 132:308664

AB A method for converting an epoxy or hydroxy moiety to a 1-deoxy-2-keto moiety is described which includes: (1) reacting a compd. having an epoxy or hydroxy moiety with a thiophenol and (2) irradiating the 1-phenylthio-2-hydroxy moiety with UV or near-UV radiation to convert the 1-phenylsulfide-2-hydroxy moiety to a 1-deoxy-2-keto moiety. The process was used to modify the cyclic peptide ring system of an echinocandin-type compd. contg. a 1,2-diol moiety to produce new keto analogs.

RX(1) OF 3 **A** + B ===> C...

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



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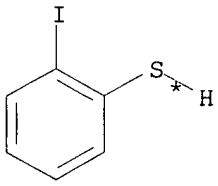
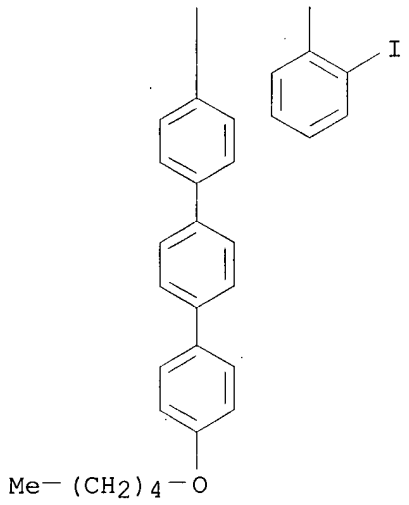


B

(1) ⟶

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



C

RX(1) RCT A **166663-25-8**, B 37972-89-7
PRO C 266317-25-3
SOL 75-05-8 MeCN, 67-56-1 MeOH
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 6 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:322923 CASREACT
TITLE: A process for the conversion of echinocandin class of peptides to their C4-homotyrosine monodeoxy analogs
INVENTOR(S): Mukhopadhyay, Triptikumar; Jayvanti, Kenia; Kumar, Erra Koteswara Satya Vijaya
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955727	A1	19991104	WO 1999-EP2715	19990422

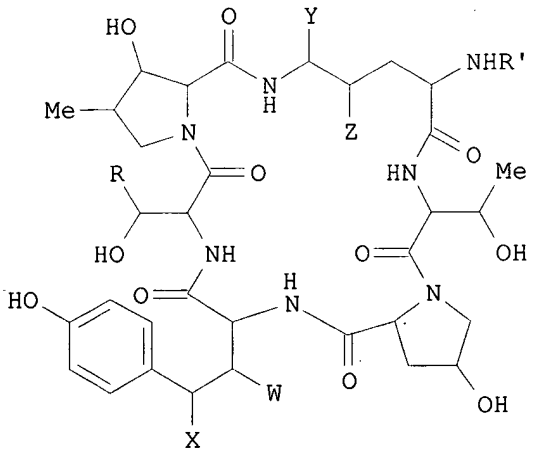
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2327474	AA	19991104	CA 1999-2327474	19990422
AU 9937096	A1	19991116	AU 1999-37096	19990422
BR 9909853	A	20001219	BR 1999-9853	19990422
EP 1073675	A1	20010207	EP 1999-919261	19990422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002513033	T2	20020508	JP 2000-545885	19990422
NO 2000005258	A	20001019	NO 2000-5258	20001019
PRIORITY APPLN. INFO.:			EP 1998-107397	19980423
			WO 1999-EP2715	19990422

OTHER SOURCE(S): MARPAT 131:322923

GI



I

AB Echinocandin type peptides I (X = OH; W, Y, Z = OH, H; R = Me, CH2CONH2, H; R' = linoleoyl, 10,12-dimethylmyristoyl, 12-methyltetradecanoyl) were converted to their C4-homotyrosine (C4-htyr) monodeoxy analogs I (X = H) via a single step selective redn. of the C4-htyr hydroxyl group of echinocandins to their monodeoxy analogs under neutral conditions without prior protection/deprotection of the equally facile C5-Orn (ornithine) hydroxyl group and purifn. of the monodeoxy compd. from the crude reaction mixt. Thus, a mixt. of mulundocandin and Raney nickel in a pH 7 ethanol soln. was stirred for 3 h at room temp. to afford 30% deoxymulundocandin, following purifn. by liq.-liq. chromatog.

RX(1) OF 1 **A** ===> B

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

A

(1)


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

B
YIELD 75%

RX(1) RCT A **54651-05-7**
RGT C 7440-02-0 Ni
PRO B 71018-12-7
SOL 64-17-5 EtOH
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

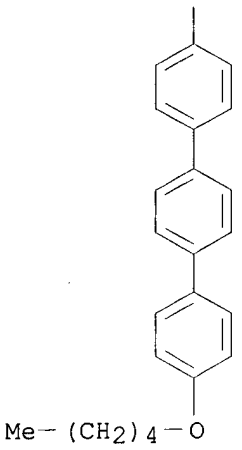
L53 ANSWER 7 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 129:276286 CASREACT
TITLE: Studies on the phosphorylation of LY303366
AUTHOR(S): Udodong, Uko E.; Turner, William W.; Astelford, Bret A.; Brown, Frank, Jr.; Clayton, Marcella T.; Dunlap, Steven E.; Frank, Scott A.; Grutsch, John L.; LaGrandeur, Lisa M.; Verral, Daniel E.; Werner, John A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Tetrahedron Letters (1998), 39(34), 6115-6118
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

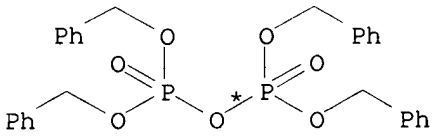
AB Phosphorylation of LY303366 was studied in THF and DMF. Benzyl phosphate (I) could be prepd. in excellent yield using LiOH as the base. Both I and the derived phosphonic acid monosodium salt were prone to undergo hydrolytic dephosphorylation.

RX(1) OF 1 **A** + B ===> C

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



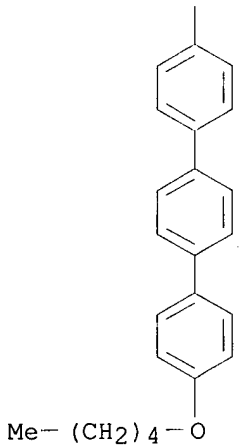
A



B

(1)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



C
YIELD 33%

RX(1) RCT A **166663-25-8**, B 990-91-0
RGT D 1310-65-2 LiOH
PRO C 213669-65-9
SOL 75-09-2 CH2Cl2, 109-99-9 THF
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 8 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 126:212437 CASREACT
TITLE: Preparation of cyclic peptide antifungal agents
INVENTOR(S): Rodriguez, Michael John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 757058	A1	19970205	EP 1996-305345	19960722
EP 757058	B1	20001108		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5629289	A	19970513	US 1995-506790	19950725
AT 197460	E	20001111	AT 1996-305345	19960722
ES 2151638	T3	20010101	ES 1996-305345	19960722
WO 9705163	A1	19970213	WO 1996-US12111	19960723
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR,				

TT, UA, UG, US, UZ
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

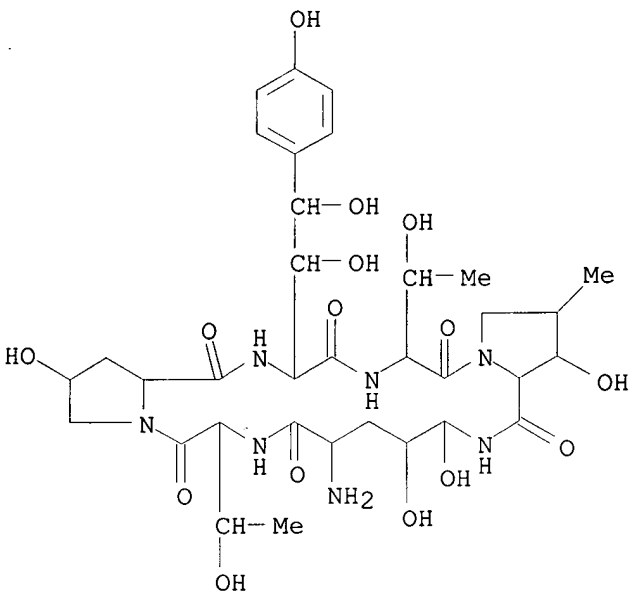
AU 9665938	A1	19970226	AU 1996-65938	19960723
JP 11510165	T2	19990907	JP 1996-507687	19960723
PRIORITY APPLN. INFO.:			US 1995-506790	19950725
			WO 1996-US12111	19960723

OTHER SOURCE(S): MARPAT 126:212437
GI

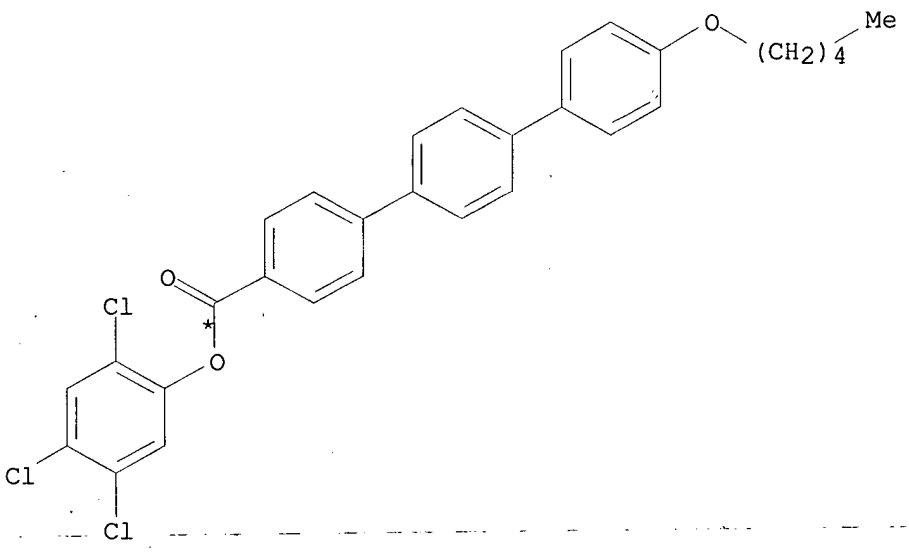
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Provided are pharmaceutical formulations, and methods of inhibiting fungal and parasitic activity using cyclopeptides I [R11 = H, CH2OH, CHMeOH, CH(OH)CH2CONH2; R12 = H, CH2OH, CHMeOH; R13 = H, Me; R31 = H, OH, OR30; R30 = C1-6 alkyl, PhCH2, (CH2)2SiMe3, CH2CH:CH2, CH2CH(OH)CH2OH, (CH2)aCO2H, (CH2)bNR41R42, (CH2)cPOR43R44, (CH2CH2O)d(C1-6)alkyl; a, b, c = 1-6; R41, R42 = H, C1-6 alkyl; R41R42 = (CH2)e; R43, R44 = OH, C1-6 alkoxy; d = 1, 2; e = 3-5; R32, R21, R22, R23, R24 = OH, H; R0 = OH, OPO3H2, OP(O)(OH)R1, OP(O)(OH)OR1, R1 = C1-6 alkyl, Ph, p-halophenyl, p-nitrophenyl, PhCH2, p-halobenzyl, p-nitrobenzyl; R2 = COC6H4R3; R3 = C6H4R5-4, C.tplbond.CC6H4R6-4, p-C6H4C.tplbond.CC6H4R7-4, p-C6H4C6H4R8-4; R5, R6, R7, R8 = H, C1-12 alkyl, C2-12 alkynyl, C1-12 alkoxy, C1-12 alkylthio, halo, O(CH2)m[O(CH2)n]pO(C1-12 alkyl), O(CH2)qXR4; m = 2-4; n = 2-4; p = 0, 1; q = 2-4; X = pyrrolidino, piperidino, piperazino; R4 = H, C1-12 alkyl, C3-12 cycloalkyl, benzyl, C3-12 cycloalkylmethyl; with the proviso that at least 1 of R11 and R12 must be H] or pharmaceutically acceptable salt thereof. Thus, acylation of 348.1 g (60.2 mmol) antibiotic A 30912A nucleus with 26.0 g (48.2 mmol) terphenyl active ester Me(CH2)4O-p-C6H4-p-C6H4-p-C6H4CO2C6H2Cl3-2,4,5 in 8.5 L of DMF gave 18 g acylated deriv. II (R11 = R12 = CHMeOH, R31 = R32 = OH) (III). Treatment of 5 g III with 17 mL CF3CO2H and 35 mL Et3SiH in 250 mL CH2Cl2 gave 3.872 g (79%) reduced deriv. II (R11 = R12 = CHMeOH, R31 = R32 = H), which underwent retro-aldol condensation by treatment with 2.51 g (22.6 mmol) Me3N+O- in 20 mL of a 1:1 mixt. of MeCN and DMF at 100.degree. for 24 h to give 72% II (R11 = R12 = R31 = R32 = H). Pharmaceutical formulations contg. II (R11 = R12 = R31 = R32 = H) arte given.

RX(1) OF 6 A + B ===> **C**...



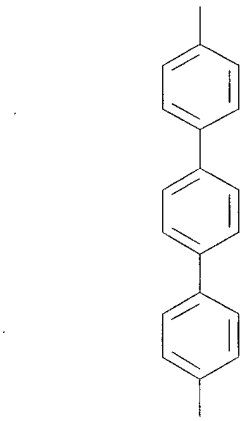
A



B

(1)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



C

RX(1) RCT A 79411-15-7, B 158937-65-6
PRO C **166663-25-8**
SOL 68-12-2 DMF

L53 ANSWER 9 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 125:115162 CASREACT
TITLE: Process for performing retro-aldol reactions using amine oxide agents
INVENTOR(S): Rodriguez, Michael John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

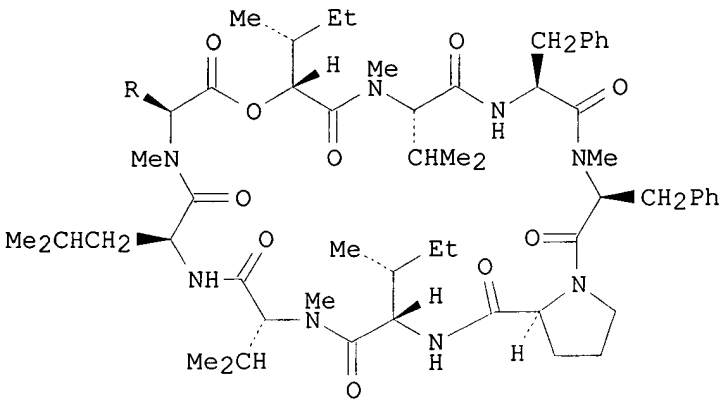
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615142	A1	19960523	WO 1995-US14613	19951113
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2205369	AA	19960523	CA 1995-2205369	19951113
AU 9641063	A1	19960606	AU 1996-41063	19951113
EP 787140	A1	19970806	EP 1995-939112	19951113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10508852	T2	19980902	JP 1995-516206	19951113
US 5677423	A	19971014	US 1996-763584	19961210

Searcher : Shears 308-4994

PRIORITY APPLN. INFO.: US 1994-339525 19941115
WO 1995-US14613 19951113

OTHER SOURCE(S): MARPAT 125:115162

GI



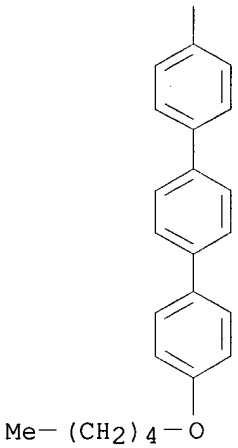
I

AB A process for removing .beta.-hydroxy groups from .beta.-hydroxy-contg. compds. id disclosed. The process involves the use of a retro-aldol-promoting reagent selected from the group consisting of trimethylamine-N-oxide, triethylamine-N-oxide, trimethylamine-N-oxide hydrate, and trimethylamine-hydrate and requires dissoln. of the substrate in an aprotic solvent and reaction under elevated temps. The process is broadly applicable to a variety of substrates including complex cyclic peptides, linear peptides, and nonpeptides. Thus, 0.25 g cyclopeptide R106-1 (I; R = CMe2OH), obtained by fermn. from Aureobasidium pullulans, was dissolved in 2.5 mL MeCN and 0.25 g trimethylamine N-oxide hydrate added all at once. The reaction mixt. was heated at 70.degree. for 24 h, cooled to room temp., concd. under vacuum, dissolved in EtOAc, washed with cold 10% HCl, satd. NaHCO3, and brine, and purified by reverse-phase preparative HPLC to yield 0.22 g (92%) of sarcosine-contg. cyclopeptide I (R = H).

RX(2) OF 3 **E** ===> F

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

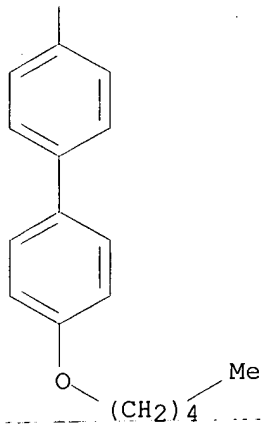


E

(2) →

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A



F

RX(2) RCT E **179118-65-1**
RGT C 136449-78-0 Methanamine, N,N-dimethyl-, N-oxide, monohydrate
PRO F 179118-66-2
SOL 75-05-8 MeCN, 68-12-2 DMF
NTE regioselective

L53 ANSWER 10 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 117:234513 CASREACT
TITLE: Reduction studies of antifungal echinocandin lipopeptides. One step conversion of echinocandin B to echinocandin C
AUTHOR(S): Balkovec, James M.; Black, Regina M.
CORPORATE SOURCE: Dep. Synth. Chem. Res., Merck Res. Lab., Rathway, NJ, 07065-0900, USA
SOURCE: Tetrahedron Letters (1992), 33(32), 4259-32
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English

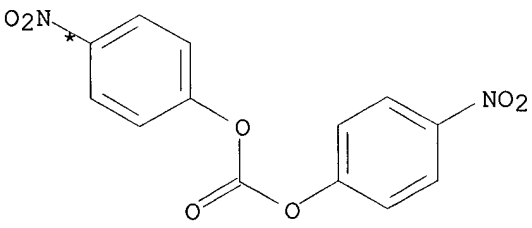
AB Sodium cyanoborohydride in trifluoroacetic acid selectively reduced the C5-hydroxyornithine and C4-hydroxyhomotyrosine carbinols to methylene groups in echinocandin lipopeptides. The selective redn. of either hydroxyl is also described. The first conversion of echinocandin B to echinocandin C was accomplished.

RX(3) OF 12 **F** + G ===> A...

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

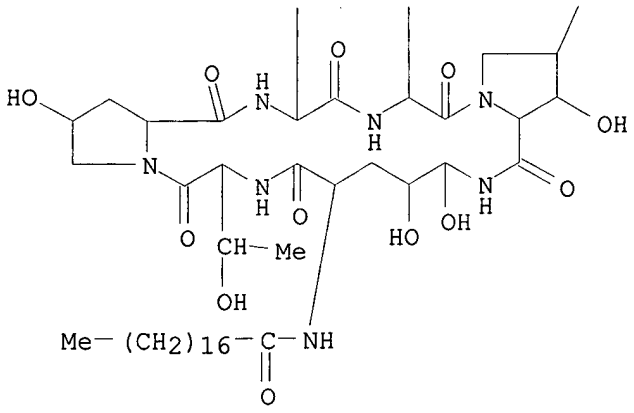
F



G

(3) →

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *



A

RX(3) RCT F **54651-06-8**, G 5070-13-3
RGT H 1310-65-2 LiOH
PRO A 144448-04-4
SOL 872-50-4 NMEP

L53 ANSWER 11 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 117:70296 CASREACT
TITLE: Preparation and structure-activity relationships of simplified analogs of the antifungal agent cilofungin: a total synthesis approach
AUTHOR(S): Zambias, Robert A.; Hammond, Milton L.; Heck, James V.; Bartizal, Ken; Trainor, Charlotte; Abruzzo, George; Schmatz, Dennis M.; Nollstadt, Karl M.
CORPORATE SOURCE: Merck Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(15), 2843-55
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
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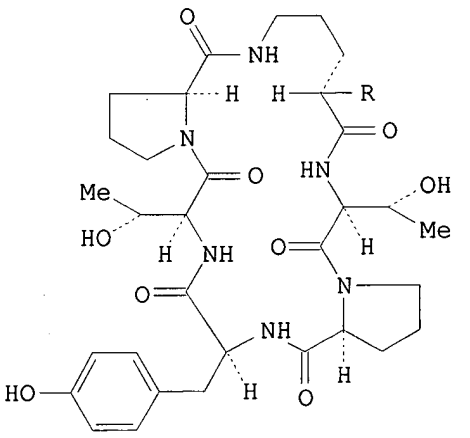


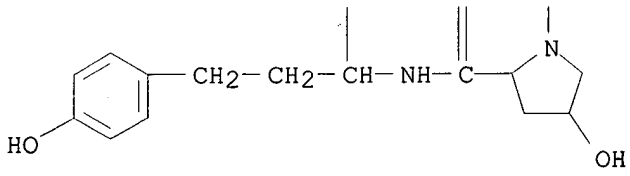
I

AB The echinocandins are a well-known class of lipopeptides characterized by their potent antifungal activity against Candida species. The mechanism of action of the echinocandins is generally thought to be the inhibition of .beta.-1,3-glucan synthesis, an important structural component in the cell wall of Candida species. Extensive structure-activity studies on the fatty acid side chain of echinocandin B led to the prepn. of the clin. candidate cilofungin. We now report the prepn., by solid-phase synthesis, of a series of simplified analogs of cilofungin in which the unusual amino acids found in the echinocandins were replaced with more readily accessible natural amino acids. The solid-phase approach to the total synthesis of these analogs allowed us to conveniently explore structural modifications that could not be accomplished by chem. modification of the natural product. The simplest analog I [R = p-[Me(CH2)7O]C6H4CONH] showed no biol. activity. Structural complexity was then returned to the system in a systematic fashion so as to reapproach the original cilofungin structure. Antifungal activity and the inhibition of .beta.-1,3-glucan synthesis were monitored at each step of the process, thereby revealing the basic structure-activity relationships of the amino acids and the minimal structural requirements for biol. activity in the echinocandin ring system. The results suggests that the 3-hydroxy-4-methylproline residue enhances activity but the L-homotyrosine residue is crucial for both antifungal activity and the inhibition of .beta.-1,3-glucan synthesis.

RX(11) OF 32 ...AE ===> **AH**

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

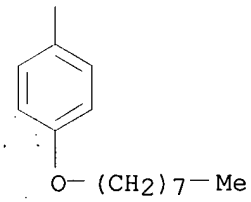


AE

(11)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

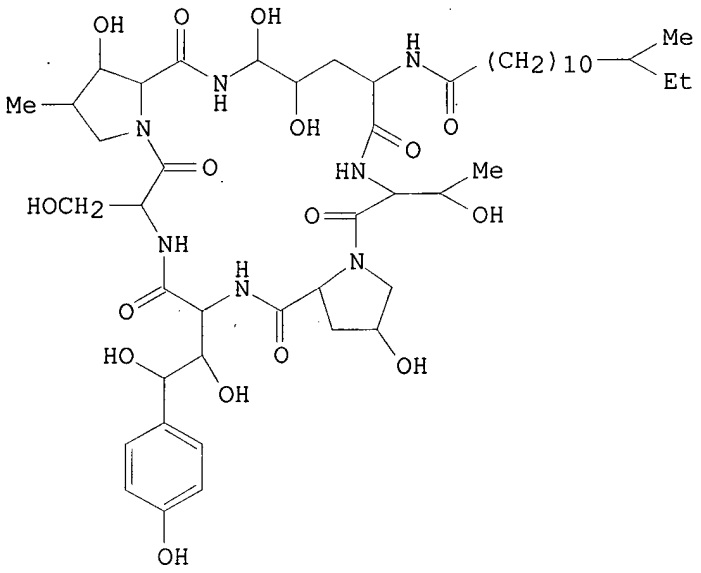
PAGE 2-A



AH
YIELD 16%

RX(11) RCT AE 141806-24-8
RGT C 26386-88-9 (PhO)2P(O)N3, D 144-55-8 NaHCO3
PRO AH **141806-25-9**
SOL 68-12-2 DMF
NTE Key step

L53 ANSWER 12 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 108:38346 CASREACT
TITLE: Mulundocandin, a new lipopeptide antibiotic. II. Structure elucidation
AUTHOR(S): Mukhopadhyay, Triptikumar; Ganguli, B. N.; Fehlhaber, H. W.; Kogler, H.; Vertesy, L.
CORPORATE SOURCE: Res. Cent., Hoechst India Ltd., Bombay, 400 080, India
SOURCE: J. Antibiot. (1987), 40(3), 281-9
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

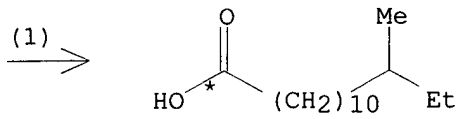
AB Mulundocandin, a new antifungal antibiotic, was shown to have structure I by high field NMR expts., e.g., homo- and heteronuclear correlation spectra, distortionless enhancement by polarization transfer (DEPT) spectra as well as nuclear Overhauser effect. The compd. is a lipopeptide belonging to the echinocandin class.

RX(1) OF 5 **A** ===> B...

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-A

A



B

RX(1) RCT A **108351-20-8**
RGT C 7647-01-0 HCl
PRO B 5502-94-3
SOL 7732-18-5 Water

L53 ANSWER 13 OF 14 CASREACT COPYRIGHT 2002 ACS

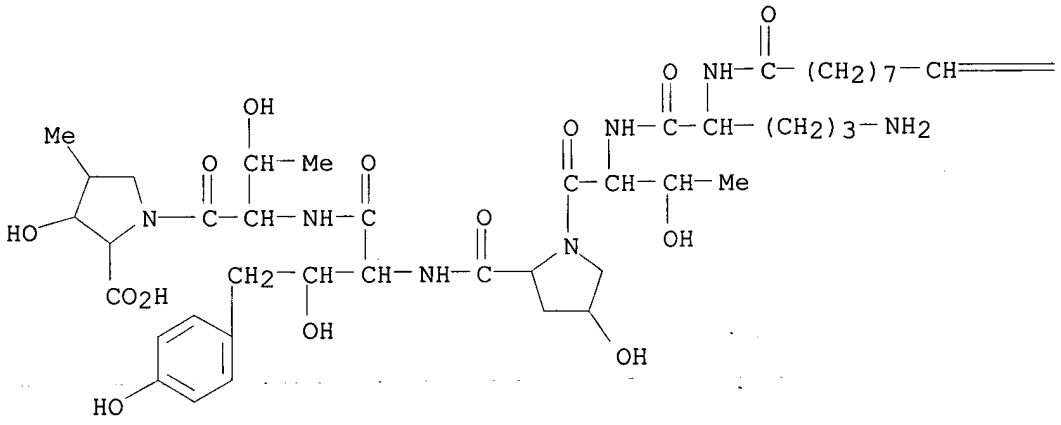
ACCESSION NUMBER: 107:237279 CASREACT
TITLE: Synthesis of the cyclic hexapeptide echinocandin D. New approaches to the asymmetric synthesis of .beta.-hydroxy .alpha.-amino acids
AUTHOR(S): Evans, David A.; Weber, Ann E.
CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: J. Am. Chem. Soc. (1987), 109(23), 7151-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total synthesis of echinocandin D (I, Lin = linoleyl) was achieved using asym. glycine enolate aldol methodol. for the prepn. of 2 constituent .beta.-hydroxy amino acids. Protected hydroxy amino acids II and III were prepd. in 4 steps each from oxazolidinones IV (R = CH2Ph, R1 = H, R2 = NCS) and IV (R = H, R1 = CH2Ph, R2 = Br), resp. In both prepns., asym. aldol addn. was used to establish the abs. stereochem. relationships at both OH and N-bearing asym. centers. II and III were integrated into the synthesis of I.

RX(1) OF 177 ...A ===> **B**...

PAGE 1-A



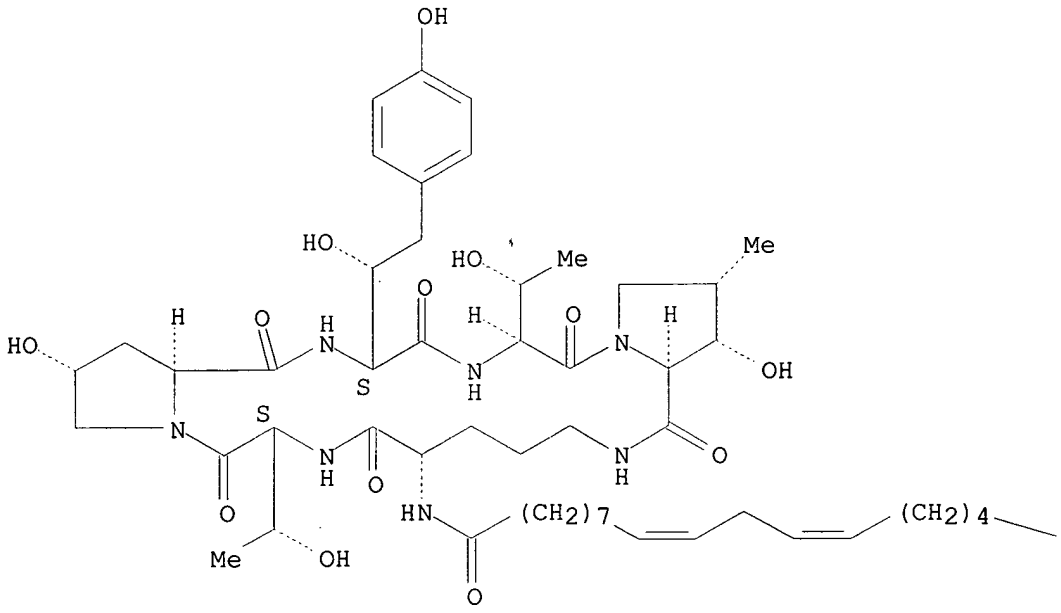
PAGE 1-B

$=CH-CH_2-CH=CH-(CH_2)_4-Me$

A

(1) →

PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(1) RCT A 104197-62-8
RGT C 26386-88-9 (PhO)2P(O)N3, D 121-44-8 Et3N
PRO B **71018-13-8**
SOL 68-12-2 DMF

L53 ANSWER 14 OF 14 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 105:173030 CASREACT
TITLE: Total synthesis of echinocandins. II. Total synthesis of echinocandin D via efficient peptide coupling reactions
AUTHOR(S): Kurokawa, Natsuko; Ohfune, Yasufumi

Searcher : Shears 308-4994

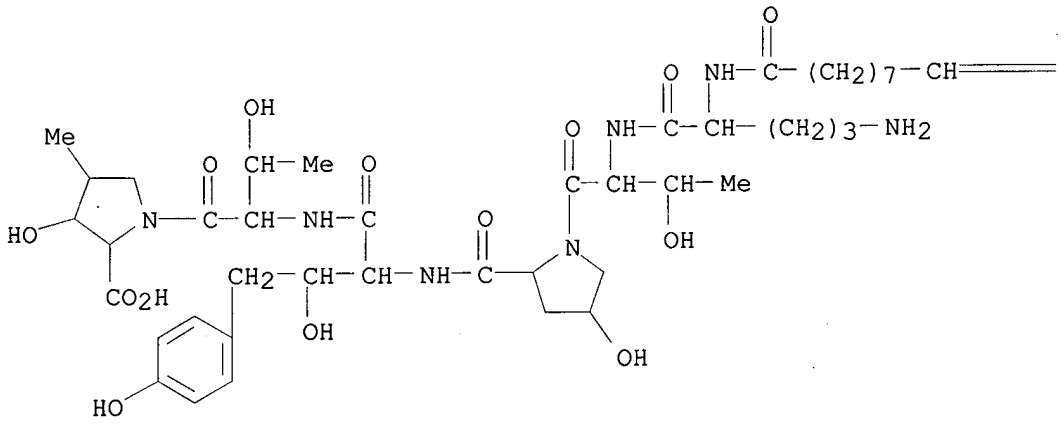
CORPORATE SOURCE: Suntory Inst. Bioorg. Res., Osaka, 618, Japan
SOURCE: J. Am. Chem. Soc. (1986), 108(19), 6043-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Echinocandin D (I, R = H) was prepd. by deblocking hexapeptide II [R = OMe, R1 = CH2NHCO2CMe3, R2 = H, R3 = Si(CMe3)Me2] (III) and cyclizing the resulting II (R = OH, R1 = CH2NH2, R2 = R3 = H) by diphenylphosphoryl azide. The deblocking of II [R = NH2, R1 = CH(OMe)2, R2 = OSi(CMe3)Me2, R3 = Si(CMe3)Me2] (IV) followed by an attempted cyclization failed to give echinocandin C (I, R = OH). III and IV were prepd. from their amino acid constituents via peptide coupling reactions.

RX(1) OF 188 ...A ===> **B**...

PAGE 1-A

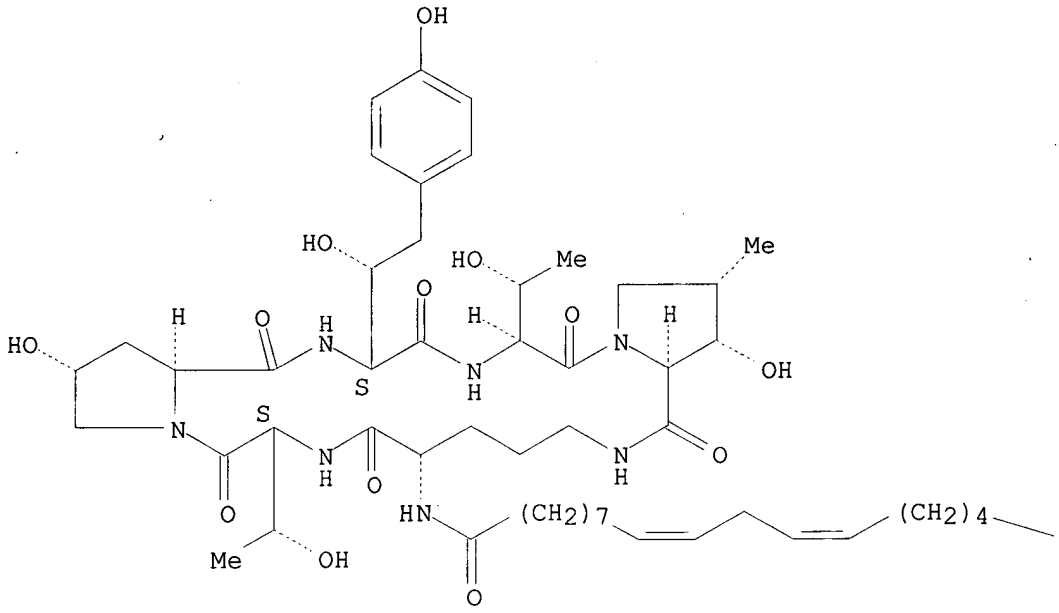


PAGE 1-B

=CH-CH2-CH=CH-(CH2)4-Me

A

(1)



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(1) RCT A 104197-62-8
RGT C 26386-88-9 (PhO)2P(O)N3
PRO B **71018-13-8**

=> fil djsmds,cheminfo,chemreact
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COPYRIGHT (C) 2002 THOMSON DERWENT

FILE 'CHEMINFORMRX' ENTERED AT 12:48:29 ON 17 OCT 2002
COPYRIGHT (C) FIZ-CHEMIE BERLIN

FILE 'CHEMREACT' ENTERED AT 12:48:29 ON 17 OCT 2002
COPYRIGHT (C) Springer-Verlag/InfoChem GmbH (IC)

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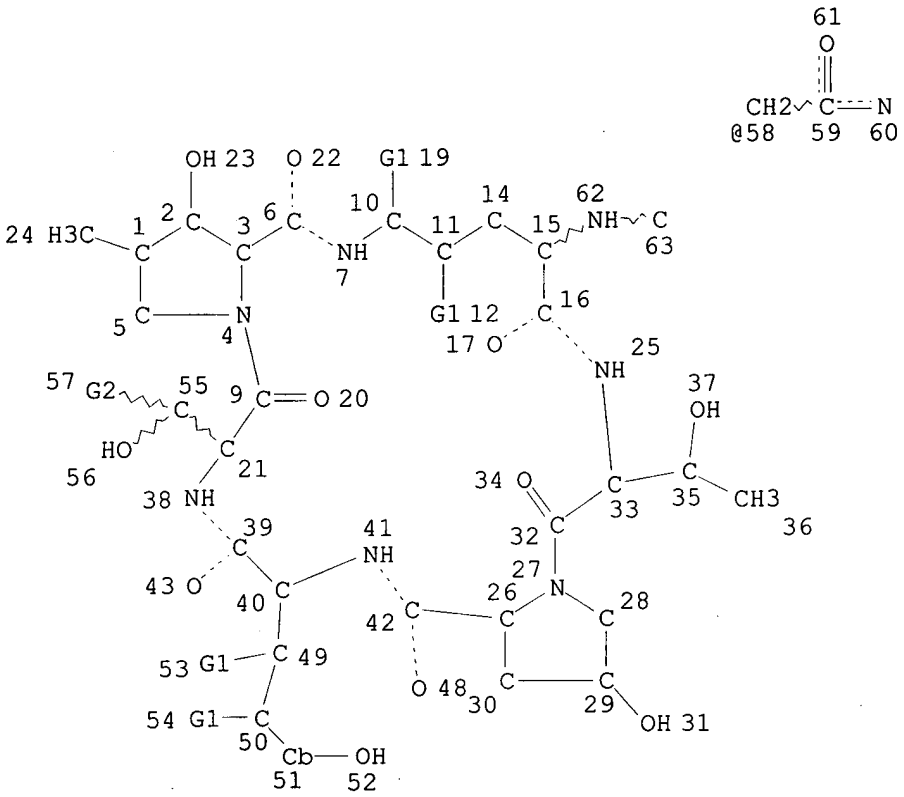
L22 STR



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GGCAT IS UNS AT 51
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE

L54 1 SEA L52

L54 ANSWER 1 OF 1 CHEMREACT COPYRIGHT 2002 SPRINGER/IC
AN 1417229 CHEMREACT
DN 88011612
AU EVANS DAVID A.; WEBER ANN E.
SO J. Am. Chem. Soc., 109, 7151-7157 (1987)
CODEN: JACSAT ISSN: 0002-7863
LA English

RX(1) OF 1 A ===> B

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

(1)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
RX(1) RCT A, 164651701
RCT.STE: S,S,S,S,R,S,R,S,R,S,R,S
PRO B, **71327204**
PRO.STE: S,S,S,S,R,S,R,S,S,S,R,R
YD 50.0 %
KW IR

FILE 'REGISTRY' ENTERED AT 12:49:24 ON 17 OCT 2002
E MULUNDOCANDIN/CN 5
L55 1 SEA ABB=ON PLU=ON MULUNDOCANDIN/CN
E DEOXYMULUNDOCANDIN/CN 5
L56 1 SEA ABB=ON PLU=ON DEOXYMULUNDOCANDIN/CN

FILE 'HCAPLUS' ENTERED AT 12:49:54 ON 17 OCT 2002
L57 13 SEA ABB=ON PLU=ON L55 OR MULUNDOCANDIN
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L59 3 SEA ABB=ON PLU=ON L58 NOT L41

- key terms claim 2

L59 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:255768 HCAPLUS
DOCUMENT NUMBER: 137:201573
TITLE: Synthesis of new echinocandin derivatives via a diol-keto transposition
AUTHOR(S): Aszodi, Jozsef; Fauveau, Patrick; Melon-Manguer, Dominique; Ehlers, Eberhard; Schio, Laurent
CORPORATE SOURCE: Medicinal Chemistry, Aventis Pharma, Romainville, F-93235, Fr.
SOURCE: Tetrahedron Letters (2002), 43(16), 2953-2956
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new diol-carbonyl transposition reaction has been discovered in echinocandin type structures. An .alpha.-hydroxy hemiaminal moiety has been shown to undergo a pinacol-type rearrangement in the presence of trimethylsilyl iodide to afford ketone derivs. Applied to **deoxymulundocandin**, this transposition led to a useful intermediate for further chem. modification.
IT **108351-20-8, Mulundocandin 138626-63-8, Deoxymulundocandin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of in the prepn. of **deoxymulundocandin** derivs. via diol-carbonyl transposition reaction)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:618023 HCAPLUS
DOCUMENT NUMBER: 135:180953
TITLE: Preparation of novel echinocandin derivatives as

fungicides

INVENTOR(S): Courtin, Olivier; Dussarat, Arlette; Melon-Manguer, Dominique; Schio, Laurent

PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.

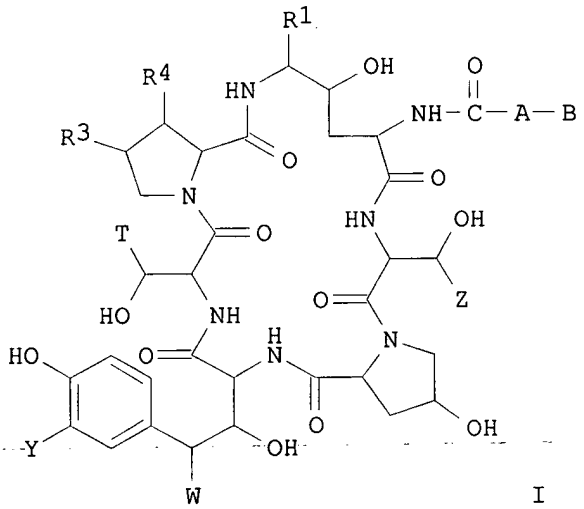
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060845	A1	20010823	WO 2001-FR419	20010214
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2804957	A1	20010817	FR 2000-1844	20000215

PRIORITY APPLN. INFO.: FR 2000-1844 A 20000215
OTHER SOURCE(S): MARPAT 135:180953

GI



I

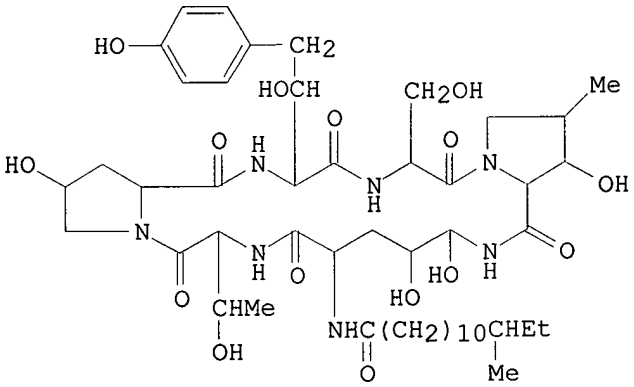
AB Echinocandin derivs. I [R1 = H, OH, (un)substituted alkoxy, alkenyloxy or alkynyloxy; R3 = H, Me, OH; R4, W = H, OH; A = O, CH2, NH; B is a steroid residue; T = H, Me, CH2CONH2, CH2C.tplbond.N, (CH2)2NH2 or alkylaminoethyl; Y = H, OH, halo, OSO3H or salts; Z = H, Me] were prepd. as antifungal agents. Thus, 1-[(4R,5R)-4,5-dihydroxy-N2-[[[(3.beta.,22E)-ergosta-5,7,22-trien-3-

yl]oxy]carbonyl]-L-ornithine]**deoxymulundocandin** was prepd. by treating ergosterol with diphosgene in CH2Cl2 in the presence of Et3N and treating the product with **deoxymulundocandin**.

IT **108351-20-8, Mulundocandin 138626-63-8, Deoxymulundocandin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of novel echinocandin derivs. as fungicides)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:527867 HCAPLUS
DOCUMENT NUMBER: 117:127867
TITLE: **Deoxymulundocandin**-a new echinocandin type antifungal antibiotic
AUTHOR(S): Mukhopadhyay, Triptikumar; Roy, Kirity; Bhat, R. G.; Sawant, S. N.; Blumbach, J.; Ganguli, B. N.; Fehlhaver, H. W.; Kogler, H.
CORPORATE SOURCE: Res. Cent., Hoechst India Ltd., Bombay, 400 080, India
SOURCE: Journal of Antibiotics (1992), 45(5), 618-23
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A new echinocandin type antifungal antibiotic, **deoxymulundocandin** (I), C48H77N7O15, was isolated from the culture filtrate and mycelia of a fungal culture, Aspergillus sydowii (Bainier and Sartory) Thom and Church var. nov. mulundensis Roy (Culture No. Y-30462). Its structure was established by comparative GC-MS analyses of the derivatized acid hydrolyzates of **deoxymulundocandin** and **mulundocandin** as well as by the high field NMR expts. (COSY, NOESY and DEPT).

IT **138626-63-8, Deoxymulundocandin**
RL: BIOL (Biological study)
(antifungal antibiotic, from Aspergillus sydowii)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, CONFSCI, SCISEARCH, GBNB, CIN, CEN, CASREACT, CHEMINFORMRX, CHEMREACT, DGSMDS' ENTERED AT 12:52:08 ON 17 OCT 2002)
L60 7 S L58
L61 3 DUP REM L60 (4 DUPLICATES REMOVED)

L61 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2002:389532 SCISEARCH
THE GENUINE ARTICLE: 545TP
TITLE: Synthesis of new echinocandin derivatives via a diol-keto transposition
AUTHOR: Aszodi J; Fauveau P; Melon-Manguer D; Ehlers E; Schio L (Reprint)
CORPORATE SOURCE: Aventis Pharma, Med Chem, 102 Route Noisy, F-93235 Romainville, France (Reprint); Aventis Pharma, Med Chem, F-93235 Romainville, France; Aventis Pharma, Process Dev Biochem, Biol Sud, D-65956 Frankfurt, Germany
COUNTRY OF AUTHOR: France; Germany
SOURCE: TETRAHEDRON LETTERS, (15 APR 2002) Vol. 43, No. 16, pp. 2953-2956.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0040-4039.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 22
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A new diol-carbonyl transposition reaction has been discovered in echinocandin tape structures. All alpha-hydroxy hemiaminal moiety has been shown to undergo a pinacol-type rearrangement in the presence of trimethylsilyl iodide to afford ketone derivatives, Applied to **deoxymulundocandin**. this transposition led to a useful intermediate for further chemical modification.

L61 ANSWER 2 OF 3 CASREACT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:322923 CASREACT
TITLE: A process for the conversion of echinocandin class of peptides to their C4-homotyrosine monodeoxy analogs
INVENTOR(S): Mukhopadhyay, Triptikumar; Jayvanti, Kenia; Kumar, Erra Koteswara Satya Vijaya
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

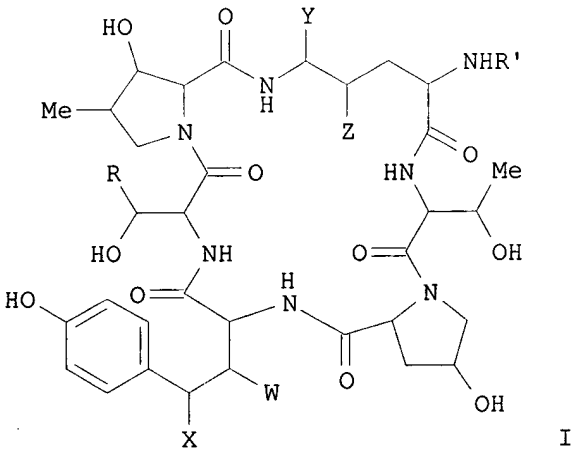
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955727	A1	19991104	WO 1999-EP2715	19990422

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,

IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2327474	AA	19991104	CA 1999-2327474	19990422
AU 9937096	A1	19991116	AU 1999-37096	19990422
BR 9909853	A	20001219	BR 1999-9853	19990422
EP 1073675	A1	20010207	EP 1999-919261	19990422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002513033	T2	20020508	JP 2000-545885	19990422
NO 2000005258	A	20001019	NO 2000-5258	20001019
PRIORITY APPLN. INFO.:			EP 1998-107397	19980423
			WO 1999-EP2715	19990422

OTHER SOURCE(S): MARPAT 131:322923
GI



I

AB Echinocandin type peptides I (X = OH; W, Y, Z = OH, H; R = Me, CH2CONH2, H; R' = linoleoyl, 10,12-dimethylmyristoyl, 12-methyltetradecanoyl) were converted to their C4-homotyrosine (C4-htyr) monodeoxy analogs I (X = H) via a single step selective redn. of the C4-htyr hydroxyl group of echinocandins to their monodeoxy analogs under neutral conditions without prior protection/deprotection of the equally facile C5-Orn (ornithine) hydroxyl group and purifn. of the monodeoxy compd. from the crude reaction mixt. Thus, a mixt. of **mulundocandin** and Raney nickel in a pH 7 ethanol soln. was stirred for 3 h at room temp. to afford 30% **deoxymulundocandin**, following purifn. by liq.-liq. chromatog.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 92324937 MEDLINE

DOCUMENT NUMBER: 92324937 PubMed ID: 1624363
TITLE: **Deoxymulundocandin**--a new echinocandin type antifungal antibiotic.
AUTHOR: Mukhopadhyay T; Roy K; Bhat R G; Sawant S N; Blumbach J; Ganguli B N; Fehlhaber H W; Kogler H
CORPORATE SOURCE: Microbiology Department, Hoechst India Limited, Mulund, Bombay.
SOURCE: JOURNAL OF ANTIBIOTICS, (1992 May) 45 (5) 618-23. Journal code: 0151115. ISSN: 0021-8820.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920821
Last Updated on STN: 19920821
Entered Medline: 19920813

AB A new echinocandin type antifungal antibiotic, **deoxymulundocandin**, C48H77N7O15, was isolated from the culture filtrate and mycelia of a fungal culture, Aspergillus sydowii (Bainier and Sartory) Thom and Church var. nov. mulundensis Roy (Culture No. Y-30462). The structure was established by comparative GC-MS analyses of the derivatized acid hydrolysates of **deoxymulundocandin** and **mulundocandin** as well as by the high field NMR experiments (COSY, NOESY and DEPT).

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